Ontario

75

ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS.

HASTREITER
In Ch.

Hearing held
8th floor
180 Dundas Street West
Toronto, Ontario

The Honourable Mr. Justice S.G.M. Grange	Commissioner
P.S.A. Lamek, Q.C.	Counsel
E.A. Cronk	Associate Counsel
Thomas Millar	Administrator

Transcript of evidence
for

December 5, 1983

VOLUME 75

OFFICIAL COURT REPORTERS

Angus, Stonehouse & Co. Ltd.,
14 Carlton Street, 7th Floor,
Toronto, Ontario M5B 1J2

595-1065

ANGUS, STONEHOUSE & CO. LTD
TORONTO, ONTARIO

ROYAL COMMISSION OF INQUIRY INTO CERTAIN DEATHS AT THE HOSPITAL FOR SICK CHILDREN AND RELATED MATTERS.

Hearing held on the 8th Floor, 180 Dundas Street West, Toronto, Ontario, on Monday, the 5th day of December, 1983.

- - - - -

THE HONOURABLE MR. JUSTICE S.G.M. GRANGE - Commissioner

THOMAS MILLAR - Administrator

MURRAY R. ELLIOT - Registrar

- - - - -

APPEARANCES:

P.S.A. LAMEK, Q.C.) E. CRONK)	Commission Counsel
D. HUNT) L. CECCHETTO)	Counsel for the Attorney General and Solicitor General of Ontario (Crown Attorneys and Coroner's Office)
I.G. SCOTT, Q.C.) M. THOMSON) R. BATTY)	Counsel for The Hospital for Sick Children
D. YOUNG	Counsel for The Metropolitan Toronto Police
W.N. ORTVED	Counsel for numerous Doctors at The Hospital for Sick Children
E. McINTYRE	Counsel for the Registered Nurses' Association of Ontario and 35 Registered Nurses at The Hospital for Sick Children

(Cont'd)

APPEARANCES: (Continued)

D. BROWN	Counsel for Susan Nelles - Nurse
E. FORSTER	Counsel for Phyllis Trayner - Nurse
J.A. OLAH	Counsel for Janet Brownless - R.N.A.
B. JACKMAN	Counsel for Mrs. M. Christie - R.N.A.
S. LABOW	Counsel for Mr. & Mrs. Gosselin, Mr. & Mrs. Gionas, Mr. & Mrs. Inwood, Mr. & Mrs. Turner, Mr. & Mrs. Lutes, and Mr. & Mrs. Murphy (parents of deceased children)
F.J. SHANAHAN	Counsel for Mr. & Mrs. Dominic Lombardo (parents of deceased child Stephanie Lombardo); and Heather Dawson (mother of deceased child Amber Dawson)
W.W. TOBIAS	Counsel for Mr. & Mrs. Hines (parents of deceased child Jordan Hines)
J. SHINEHOFT	Counsel for Lorie Pacsai and Kevin Garnet (parents of deceased child Kevin Pacsai)

VOLUME 75

INDEX OF WITNESSES

INDEX OF EXHIBITS

/DM /ak

---Upon commencing at 2:30 p.m.

THE COMMISSIONER: Yes, Mr. Lamek.

MR. LAMEK: Mr. Commissioner, before we begin perhaps I should say that the last two exhibits from Friday, that is to say the medical records from the St. Joseph's Hospital and the McMaster Medical Centre on Kevin Pacsai are not yet ready, but they will be copied and will be distributed very shortly.

May I please call Dr. Alois Hastreiter.

DR. ALOIS RUDOLF HASTREITER, Sworn

DIRECT EXAMINATION BY MR. LAMEK:

Q. Dr. Hastreiter, you were born as I understand it in Rio, Brazil a little over 56 years ago?

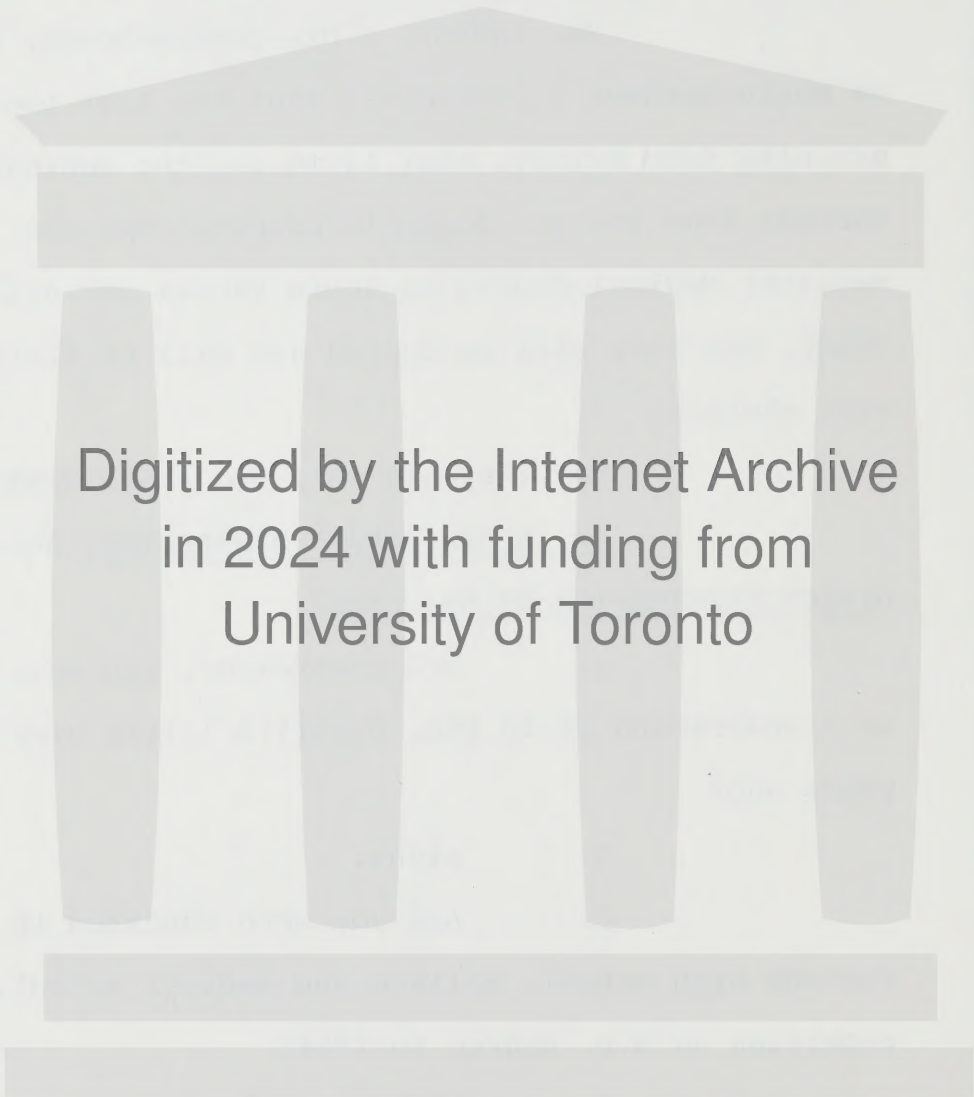
A. Right.

Q. And you were educated in Brazil through high school, college and medical school, receiving an M.D. degree in 1954?

A. Right.

Q. You subsequently interned in hospitals in Rio; and in 1955 you came to the St. Luke's Hospital, New Bedford, Massachusetts to do a rotating internship at that hospital for a year?

A. Right.



Q. Subsequently at the Philadephia General Hospital, 1958-1959, you spent a year doing a pediatric residency?

A. No, three years.

Q. I am sorry, is that three years? That's right, you were Chief Resident for the last of those three years?

A. Right.

Q. And then you did a Fellowship in Pediatric Cardiology at the Children's Memorial Hospital in Chicago, from 1959 until 1961?

A. Right.

Q. Since 1961 until 1973 you were an Associate Attending Pediatrician at Children's Memorial Hospital in Chicago?

A. It is '61 to 1963.

Q. To 1963 and then an Associate Attending Pediatrician until 1973, is that right?

A. Not at Children's Memorial.

Q. Then your CV is all wrong.

A. I moved to the University of Illinois and Cook County Hospital in 1963, and I became a member of their staff up until now.

Q. Certainly you have held academic appointments in the Department of Pediatrics

at Northwestern University since 1962 I believe?

A. Yes.

Q. And as you say, since July of 1963 you have been the Attending Physician at Cook County Hospital, and a Director of the Division of Pediatric Cardiology at the University of Illinois Hospital from September of 1967?

A. Right, up until 1982, last year.

Q. And you are a Professor of Pediatrics in the University of Illinois, Abraham Lincoln College of Medicine from September 1970 I believe.

A. Right.

Q. Do you still hold that appointment?

A. Yes.

Q. And you hold certification from the American Board of Pediatrics, by that same Board, Sub-Board of Pediatric Cardiology, do you not?

A. Right.

Q. And among a number of professional societies of which you are a member of the American College of Cardiology, you are Fellow of that College, I believe?

A. Yes.

Q. You are a Fellow of the American Academy of Pediatrics?

A. Yes.

Q. You are a member of the American Academy of Pediatrics, Cardiology Section, are you not?

A. Yes.

Q. And as I say numerous other associations, societies and foundations?

A. Yes.

Q. You have served on several committees of the Chicago Heart Association and other organizations, primarily with respect to matters involving congenital heart disease and heart disease in the young?

A. Yes.

Q. Over the years you have been a special lecturer on a variety of cardiology related topics, including of special interest to this Commission, in 1978 when you lectured on the disposition of digoxin in pre-term and term neonates at the Prenatal Program on Developmental Pharmacology at the University of Illinois. Then in November of 1978 you lectured on Drug Overdose in the Heart at the

Chicago Heart Association Nurses Workshop, University of Illinois Medical Centre?

A. Yes.

Q. And similarly, Doctor, over the years, you have presented papers and abstracts on research at professional meetings, conferences and symposiums,regularly and frequently and that is going back over a period of some 23 years I believe?

A. Yes.

Q. The first published research that I have been able to find among those listed in your curriculum vitae dealing with Digoxin was some 15 years ago. Since that time you have presented papers frequently on different aspects of digoxin therapy and toxicity, have you not?

A. Yes.

Q. I won't take the time to enumerate them, Doctor, they are listed in the curriculum vitae with which you have provided me.

I wonder, Mr. Coimissioner, if the curriculum vitae of Dr. Hastreiter might be the next exhibit, please?

THE COMMISSIONER: Yes, 280.

---EXHIBIT NO. 280: Curriculum Vitae of Dr. Alois Rudolf Hastreiter.

MR. LAMEK: Q. Now, Dr. Hastreiter, we are grateful to you for having come to give evidence at this Commission. Obviously our interest in your doing so was prompted by the fact that you were retained as a consultant to the police and to the Ministry of the Attorney General, initially with respect to the prosecution of Nurse Nelles arising out of the deaths of four children at the Hospital for Sick Children.

Could you tell me, please, when you were first approached to act as a consultant to the police in respect of their investigation?

A. In May, mid-May of 1981.

Q. By whom were you approached?

A. Initially by Dr. Tepperman, and subsequently by Jerome Wiley, the Crown Attorney.

Q. The Crown Attorney?

A. Yes.

Q. Can you tell us please what you were told about the case and what it was that Dr. Tepperman and Mr. Wiley wanted you to do for them?

A. First I was asked if I had knowledge of this case; and I had read in the papers in Chicago some news about Miss Nelles' arrest and the fact that there was a problem with a number of

babies at the Hospital for Sick Children, but I really had no knowledge of the details and they filled me in, and told me, and asked me if I would be willing to help them look into the situation from a medical standpoint, and a toxicologic standpoint, to evaluate the cases then to see, in other words, help them in the investigation basically.

Q. And were you asked to review hospital charts of children who had died in the Hospital?

A. Yes. When I accepted, I was invited to come to Toronto and I spent initially I believe two days reviewing the charts of the children and then I came several times. This is basically what I did, reviewing the charts and met with various Crown Attorneys and the Police, and members of the police force.

Q. Can you tell us, Dr. Hastreiter, initially how many charts you were asked to review?

A. I don't remember the exact number but I have the reports, my initial report is related to the charts that I reviewed, I could count them.

Q. Well, we will come to that in a moment, Doctor. I should tell you that the report

as it is found in the binder which I have provided to you and which has been provided to all counsel here and marked as an exhibit, is selective in the sense that we have eliminated from it reviews of children whose deaths are not here under investigation. So you may not be able to tell by counting the number of children in that report how many were in fact reviewed, it may have been more, you may have included children in whose deaths we are not concerned in this Commission.

A. Yes.

Q. Do you know who selected the deaths which were to be reviewed by you, and on what basis the selection was made?

A. I believe that the initial selection was done by the coroner and subsequently with the assistance of the members of the Police Board. I believe they screened them before I reviewed them.

Q. Do you know the basis upon which they selected the ones for review by you?

A. These were children that had died on the Wards 4A/4B during a specific period of time between July 1980 and March 1981, and children in whom the event of death was not totally clearly explainable on the basis of their original disease,

and the possibility of digoxin intoxication existed because of that clinical evidence.

Q. You told us, Doctor, that you were to review the charts. On that initial review, and I am thinking now of the spring of 1981, was any information other than that contained in the Hospital charts provided to you?

BB
/PS

A. No information except some of the information that the police had but that had little relationship to my work. Actually, it was more the investigation aspects of the case.

Q. We know at that stage Dr. Cimbura had not yet begun to produce results from the Centre of Forensic Sciences on digoxin assay so I take it there is no such information provided to you in May of 1981.

A. No. There were some blood levels of digoxin available. These had been performed at the hospital itself and at other hospitals like the Toronto General, I think, had confirmed one analysis, but none from the Centre for Forensic Sciences.

Q. And were such digoxin assay results that you did have contained in the charts themselves?

A. I believe that, yes, on the four children for which Nurse Nelles was eventually indicted.

Q. In carrying out your initial review --

MR. BROWN: Let's be quite clear, Nurse Nelles was discharged.

THE COMMISSIONER: Yes, I was trying

to think if there was anything wrong, though. You have to have an indictment even before there is a preliminary inquiry -- no, an indictment comes after a preliminary inquiry.

Technically you are wrong, Doctor.

THE WITNESS: Sorry.

THE COMMISSIONER: She was charged.

MR. LAMEK: She was charged.

THE WITNESS: Charged, yes. Sorry.

MR. LAMEK: Q. Two people divided by a common language, I am afraid, Doctor.

In carrying out the initial review in the spring of 1981, Dr. Hastreiter, did you confer with any physician, surgeon, pharmacologist, pathologist, biochemist from the Hospital for Sick Children?

A. In the spring of 1981, no.

Q. Or from any other institution? Did you confer with any medical person from any other source in conducting your own review, other than Dr. Tepperman and the people who retained you, of course.

A. No.

Q. Did you in the spring of 1981 have any discussions with Mr. Cimbura prior to

receiving from him any assay results?

A. I believe so, yes. We started talking possibly in the late spring, early summer.

Q. Okay.

A. But I had no data --

Q. You had no data.

A. -- available at the time.

Q. Dr. Hastreiter, we have marked as an exhibit in these hearings a bound set of your reports as they were received from the Metropolitan Toronto Police and copied.

I have provided a copy of that volume to you, and recognizing that it contains some considerable measure of duplication, do you recognize it as a compilation of reports that you prepared pursuant to your retainer as a consultant by the police and the Crown Attorney's office?

A. Yes.

Q. Thank you.

I'll tell you, Doctor, I am issuing a disclaimer. I don't claim either credit or accept blame for the sequence in which things are bound in this document.

Could I ask you to turn to Page 10 for me,please, because curiously on Page 10 there appears

to be a covering letter for your initial report.

THE COMMISSIONER: This is an exhibit, I think, is it not?

MR. LAMEK: Yes, it is.

THE COMMISSIONER: Quite recently, isn't it? Do you know the number?

MS. CRONK: 264.

MR. LAMEK: 264.

Q. That letter Dr. Hastreiter, dated May 29th, 1981, apparently from yourself to Mr. Wiley, enclosing you say in the letter a report of your analysis of 21 infant deaths at the Hospital for Sick Children, the calculation of the amount of digoxin administered to the four infants in whom post mortem blood concentrations were available -- that is to say, Cooke, Miller, Pacsai and Estrella, and also your answers to a number of questions that had been put to you by Sgt. Warr.

A. Yes.

Q. You say that you had tried to interpret the medical data as objectively as possible, but in some cases you wanted to obtain additional information.

Could we drop down to the last sentence in that paragraph, Doctor:

"With regard to Sgt. Warr,s questions, some of the answers are still incomplete and will require additional research."

And the final paragraph:

"As indicated earlier, it probably would be useful for me to spend another day or two in Toronto in the relatively near future to perform a more complete analysis and to possibly answer additional questions."

Could you tell me what, as of May 29, you needed by way of additional information or you needed to do to perform a more complete analysis? What was lacking at this stage?

A. There was some information related to these infants that I didn't have available on my first visit, and this was mostly laboratory data.

For instance, there were babies in whom the possibility of renal failure existed, but I didn't have enough laboratory data to either prove or disprove the existence of it.

Q. I see. That kind of information you needed to obtain on a further visit.

A. Yes.

Q. I will come back later, if I may, to the references in your letter to the calculation of dosages to the four children.

There follows that letter from Pages 11 to 22 reports of greater or lesser length on, as I counted, some 22 children. The letter refers to 21. Perhaps my count is in error.

Those I take it are reports that accompanied the letter of May 29, are they?

A. Yes.

Q. Then the other enclosures that are referred to in the letter are found at, first, Pages 23 to 26, which includes the calculations and the formula for calculation of dosage.

And then Pages 27 to 33 the answers to specific questions that had been addressed to you by the police.

A. Yes.

Q. We will refer to those from time to time in the course of the next day or so, Doctor.

Now, by the time we get then to Page 33 of this binder, starting at Page 10, your letter, and then going to Page 33, is that in its entirety

the initial report that you submitted under date of May 29, 1981?

A. I believe so, yes.

Q. Doctor, in approaching that review, having as you have told us very little in the way of digoxin level formation except with respect to four children, what was the object of the exercise? What were you setting out to do in reviewing those charts?

A. My function was to screen the charts for children who possibly might have received an overdose of digoxin. Since the time it was felt that some babies had received it and the possibility existed that other babies may have received it also, I was asked to advise the police and the Crown regarding the situation, the status of these specific babies. So in looking through the chart I could easily eliminate some babies. Others I could not, and in some the circumstances leading to death were such that they probably deserved a little further investigation into the situation.

Q. Were you examining the clinical picture of each child with the view to seeing if there was anything in that clinical picture as disclosed by the chart which raised a question of possible

digoxin intoxication?

A. Yes.

Q. That is essentially what you were about?

A. Yes. Basically, yes.

Q. Yes.

A. But also to eliminate the ones that were not.

Q. Yes, of course.

A. That was a very important function so we can limit the number.

Q. Do I take it if upon reading the chart you came to the conclusion that the entire clinical course including terminal event, decline and death, were all entirely explainable in your view in light of the child's clinical and disease condition, that you would probably put that one into the pile that said there was no reason to think of digoxin in this case?

5dec83
CC
BMcra

A. Except that I would have to be very certain that this was the situation.

Q. If there was anything that might call for an explanation you would put it in the pile for further explanation, I take it?

A. Yes.

Q. Now, was this report of May 29, 1981 subsequently discussed with Mr. Wiley and the police and the Coroners in Toronto?

A. Yes, we had several meetings related to children and the reports.

Q. Did those take place over the summer of 1981?

A. Yes, summer and fall also.

Q. Now, I take it as Mr. Cimbura's toxicologic data will be coming available, that information was furnished to you?

A. Yes.

Q. And on September 30, 1981 you wrote a letter which is contained at page 1 of this binder again addressed to Mr. Wiley and enclosing what you call an updated report of your findings on several infants and a couple of other matters as well?

A. Yes.

Q. I tell you, Dr. Hastreiter, we

CC2

have not included in this binder the scientific papers that were enclosed with that report. But the updated report, and I believe Mr. Cimbura's findings are included. Thereafter, on pages 2 through 8 are indeed updated reports on certain children incorporating notably certain toxicological data which presumably had been produced and furnished to you from Mr. Cimbura.

A. Yes.

Q. And those reports are upon Cook, Miller, Pacsai, Estrella and Hines. Other than the incorporation of the toxicological data which had become available and your comments upon it, was there any other reason as at the end of September 1981 to update these reports?

A. No, I believe that these were the main reasons. There was some additional information regarding laboratory data and other relatively minor information I think that helped.

Q. Yes, some of the information which you had been lacking in the spring you have now located and incorporated?

A. Yes.

Q. But I take it you were now looking, Doctor, at all of the available information

CC3

about these children including Mr. Cimbura's results and not restricting your gaze solely to the medical records, the Hospital records as you had initially, is that fair?

A. Right, yes.

Q. Now, other than the two reports to which we have just referred, Dr. Hastreiter, did you furnish any other written reports to the police or to the Crown or to the Coroners prior to the preliminary inquiry?

A. No.

Q. Okay. And at any time prior to your giving evidence at the preliminary inquiry, which was towards the end of that hearing you will remember, did you change any of the opinions expressed in the reports which you had furnished in the spring and summer of 1981?

A. No.

Q. Okay. Following the discharge of Nurse Nelles at the end of the preliminary inquiry in May of 1982, Dr. Hastreiter, did you participate in any further review of deaths at the Sick Children's Hospital in the period about which we are talking?

A. Yes, I did.

Q. When was that, please?

CC4

A. That was shortly after the discharge of Miss Nelles, we were asked to review a larger number of children and this I believe included all children who had died during that particular period from June 1980 through March 1981, and I believe that the total was 61 charts that we had to review for the same purpose of screening them for the possibility of digitalis overdose.

Q. Okay. And in the course of that, did you re-review the charts that you had looked at in the spring as well as certain additional charts?

A. Yes.

Q. And we have heard from Dr. Fay who was also involved in that exercise, as I understand it.

A. Yes.

Q. Now, I want to review that exercise at some later point and in particular the meeting that was held on September 13, 1982 and at which you were present, were you not?

A. Yes.

Q. When the review of all these charts by you and Dr. Fay was discussed and Dr. Kauffman gave his thinking on the pharmacological --

CC5

I'm sorry, no, not Dr. Kauffman, there was no pharmacologist at that time, was there?

A. No.

Q. But your review was discussed, Dr. Fay's review was discussed, there was a general polling of views among a large number of people present and deaths were categorized, you will recall.

A. Yes.

Q. Now, I may refer to that from time to time in the course of specific discussions of specific children but that was the culmination of that summer of '82 project, was it not?

A. Yes. I believe the main purpose was really to bring the clinicians and toxicologists together.

Q. Yes.

A. With Dr. Bennett presiding as the Coroner, making the decisions.

Q. Now, the reviews that you did in the summer of 1982, as I understand it, are contained in this binder at pages 34 to 89 I believe. Those are some additional children?

A. Yes.

Q. And in particular you reviewed deaths at that time which had not previously been

CC6

reviewed by you before and they were those of Belanger, Floryn, Gage, Heyworth, Leith, Lombardo, Paul Murphy, Onofre, Perreault, Shrum, Taylor, Velazquez, Volk and Woodcock. These I take it were the added starters if you will that were added to the list following the preliminary inquiry into the Nurse Nelles case?

A. I don't remember all the names.

Q. Okay.

A. But we added about 40 I believe from our previous investigation.

Q. Well, you will again understand, Doctor, that I have only included those children amongst the 36 with whom we are concerned.

A. Oh, yes, yes.

MR. ORTVED: What pages are those again, Mr. Lamek?

MR. LAMEK: I believe 34 to -- did I say 89?

THE COMMISSIONER: You said 89 but I am not sure you meant it.

THE WITNESS: This is a little out of order, unfortunately.

MR. LAMEK: Q. It is grossly out of order, unfortunately, and I am sorry about that,

CC7

Doctor. You will also find beginning at page 90 and going to page 172 a compilation of what I believe to be the same reports.

A. Yes.

Q. But including a lot of others whom you had previously reviewed.

A. Yes.

Q. And then just against the possibility that that not be enough reports, starting at page 174 and going to page I think 275 you will find the same reports all over again.

A. Right. There are three copies of them.

Q. Well, you must have impressed the police mightily, Doctor, because they produced three copies of these things and furnished them to us.

THE COMMISSIONER: Just so we will understand it, you said 34 to 89 --

MR. LAMEK: Well, perhaps 34 to 71, Mr. Commissioner, are I think the new reviewed deaths with one or two cases which had earlier been reviewed including the first one Adamo. Starting at page 72 with Justin Cook and going through to page 172 I believe you will find the summer of '82 review of all

CC8

of the children in whom we are interested.

THE COMMISSIONER: 72 to 102 did you say?

MR. LAMEK: 172. 72 to 172.

THE COMMISSIONER: Okay.

MR. LAMEK: And then again from 174 to 275,the same thing.

THE COMMISSIONER: What is the prospect of an index?

MS. CRONK: I'm sorry, sir?

THE COMMISSIONER: What are the prospects of an index?

MR. LAMEK: I thought that request had been addressed to somebody.

THE COMMISSIONER: Yes, yes,I did.

MS. CRONK: We will certainly have them done, sir.

THE COMMISSIONER: When Miss Cronk was harassed on something else, I asked for an index to this, so she gave it the attention it deserved.

MS. CRONK: I apologize, sir, they will be done.

THE COMMISSIONER: It would be nice if we had an index that will not only give us all the help that Mr. Lamek is giving us so far but will

CC9

specify within those categories each child. All right.

MR. LAMEK: Q. Doctor, it may be the easiest thing to do is, for the purpose of this summer of '82 review, to look at the section form page 72 to 172. That I think included all the children in whom we are interested.

For this review, it appears a form was devised setting out the information which presumably is felt to be relevant. Did you design the form?

A. Yes.

Q. And it appaars here as a two-page form. As I understand it, it was a two-sided form?

A. Right.

Q. Setting out first the history and hospital course and diagnosis information and on the back of it the laboratory, biochemistry results, that sort of thing.

A. Yes.

Q. And then as I read it too, looking for example at Justin Cook's review, it starts at page 72, following that is a copy of the report which you had earlier done, the narrative report on Justin Cook and I take it in some cases those may have

CC10

been updated or varied slightly in the course of the '82 review?

A. Yes.

OD/DM/ak

Q. Could we look at the Justin Cook documentation at page 72, please. After setting out what I call the statistical information; date of birth; date of admission and so on; time of death and that sort of thing and the history of the Hospital course, diagnosis and cause of death. The bottom item on the page is: "Probability of Massive Digoxin Overdose", then three boxes, "Small", "Fair" and "Good".

In the case of Justin Cook you seem to indicate that there was a fair probability in this baby's case of massive digoxin overdose.

Now I tell you that on the face of it that seems rather at odds with what we have heard in this Commission so far. Can you tell me on what basis you assessed the probabilities of massive digoxin overdose in Justin Cook's case as being "fair"?

A. Yes. This evaluation was done completely on clinical grounds, not including the toxicological evidence that we had. Since most babies did not have any toxicologic evidence we wanted to compare the clinical status of all these babies. So in those that we had toxicology we tried to forget about it for the classification and categorization.

DD2

I should also say perhaps that the reason for this was to screen the babies who were candidates for digoxin overdose. And the categories mean really that the ones that are classified as "small", small probability, means that they were excluded completely. The ones that were classified as "fair" were included but had a low probability. The ones that were classified as "good" were included and had a higher probability.

Q. If I understand this correctly then, the assessment at the bottom of the page was based solely on the clinical picture as revealed by the chart and took no account of toxicological information?

A. Right.

Q. And it was only in getting to the narrative portion of the report that you referred to and incorporated into your appraisal such toxicological data as were available?

A. Yes.

Q. I am just interested in one word before we leave that, Doctor. Why "massive digoxin overdose", and please how much is "massive"? What do you mean by that category?

DD3

A. Well the term "massive" has been employed for fatal intoxications. We usually divide digoxin, digitalis intoxication into two groups one would be the therapeutic overdose, and the other would be either accidental or purposefully administration of an overdose, and this is usually classified as massive often in the literature, it takes a very large dose to kill somebody.

Q. Since your interest was in those children whose deaths may have been caused by digoxin overdose, you selected massive to describe, to measure the overdose that you were interested in discerning?

A. Yes, because we were not interested in mild signs of intoxication, which is a frequent situation in a clinical setting.

Q. Now, with respect to the review that you conducted in the summer of 1982, did you consider any other data or information other than the information contained in the Hospital record and the toxicological information that was available from Mr. Cimbura?

A. No, that was basically all.

THE COMMISSIONER: I am sorry, I thought that Dr. Hastreiter said - well, may have

DD4

considered it, but certainly in calculating the probability you ignored it, isn't that right?

THE WITNESS: Yes.

MR. LAMEK: I meant in the overall review, Mr. Commissioner.

THE COMMISSIONER: Yes.

MR. LAMEK: Q. It was really a sort of two stage review of each child as I have understood you, Dr. Hastreiter. First on a purely clinical basis without reference to the toxicological data; and then second, incorporating such toxicological data as there were available.

A. Right.

Q. You have told me that this was the last chart review that you performed for the police, the Crown Attorneys and the Coroners?

A. Yes.

Q. And therefore when I come to page 173 of this chart and find Dr. A. Hastreiter's second review, what I am really seeing is the second copy of your summer of 1982 review?

A. Yes.

Q. In a sense that was the second review following the preliminary inquiry?

A. Yes.

DD5

Q. You have told me, Dr. Hastreiter, that when you did your initial review in May of 1981, other than the post mortem digoxin levels on the four children, Cook, Miller, Pacsai and Estrella, you did not have any other toxicological information and therefore you didn't worry about being influenced by that kind of data when reviewing the clinical record?

A. That's right.

Q. You have also told me that in the summer of 1982 part of it was to set aside anything you knew, if you could, about toxicological data, and again concentrating on the clinical picture, that was part of the exercise in the summer of 1982.

A. That was after the preliminary hearing?

Q. Yes.

A. Yes.

Q. In considering whether the clinical picture raised questions as to the possible involvement of digoxin in the death of a child, did you also consider whether it raised questions as to the involvement of any other agency in the death of the child; another drug, or some other kind of intervention, or were you just focusing on the possibility of digoxin intervention?

DD6

A. I was just focusing on digoxin. However, I only considered other drugs to the extent that they might occasionally interfere with digoxin either with the action of digoxin or with the assay of digoxin, or its measurement in the blood, only in that respect did I consider other drugs.

Q. In conducting the review at either stage - well, let's focus on the first one first. 1981; in 1981, in conducting your review of these charts, did you take any cognizance of the fact that many of these children had died in the early hours of the morning, were you aware of that at the time you did your initial review?

A. No, I was not.

Q. And therefore could not have been influenced by that?

A. I only became aware of that considerably later.

Q. Were you aware of that by the time you came to do your 1982 review, after the preliminary inquiry?

A. Yes, I was, because this had been brought up at the preliminary hearing; but then Dr. Bryson made a statistical study and it became

DD7

clearer to me then.

Q. In conducting your second review in 1982, being now aware that there was a significant number of deaths which had occurred in the early hours of the morning, sort of time clustering if I may between 1 o'clock and 5 o'clock in the morning, did you take any conscious cognizance of that in assessing the possibility of digoxin involvement in any of these deaths?

A. No, not really. I had no interest in this particular aspect, I was only concerned with the medical aspect of these cases.

Q. Were you aware in 1981, when you did your review, that many of these deaths had occurred in the presence of a particular nursing team?

A. I became aware of it again at the - actually prior to the preliminary hearing, from my meetings with the police members, the members of the police force and the Crown, but I didn't feel that this had any influence on what I was doing.

Q. I noticed, for example, going back to your initial report, Doctor; let me find an example, page 15, a bad example, but I will come back to that. Page 11, with respect to Cook, the very

last comment you make upon Cook after a review of the chart:

"The medical record appears to indicate that Miss Nelles was caring for the infant at that time."

That is to say at the time of the terminal episode of the child. That I take it was a non-medical fact that you were drawing from the chart?

A. That is correct. In my first review I had specifically been asked about the possibility of this baby being poisoned with digoxin, and I think the time element was very important, so it was important; and since I had specifically been asked about Miss Nelles I think I did connect her and her presence or absence with this investigation, mainly because of the time connection to see if the feasibility of administration of drug had occurred in this particular case.

Q. So far as you are aware, Doctor, and I ask you no more than that, so far as you are aware did the presence or absence of Miss Nelles at the time any child got into difficulties have any influence upon your assessment of the likelihood of digoxin intoxication in that child's death?

A. No, I don't believe so.

Q. Perhaps you can help us on this then; what kind of matters were you looking for in the clinical picture of a child which might be suggestive of digoxin intoxication?

A. I think the main fact that I was looking for was whether or not this child's death was explainable on the basis of the child's original problem. Digoxin intoxication has no specific symptoms. There are symptoms which may suggest it, but there are no symptoms really that will prove its existence. Therefore, I tried to put the symptoms together because this would help strengthen the case perhaps a little. The main evidence was really whether or not the child suddenly deteriorated, the suddenness of the episode I think was important to whether there was a sudden deterioration in the child's clinical condition and whether of not this was explainable on the basis of the child's disease, original heart condition.

Q. If I understand you you were looking for those symptoms which although not specific to digoxin toxicity may indicate it, or are consistent with it; and you were looking for deaths, in particular sudden onset of symptoms, which did not appear to be explained readily by the

child's clinical condition and course, is that fair?

A. Right.

Q. You seem to place some importance on the sudden onset of critical symptoms, the sudden decline or deterioration of the child, is there anything unusual about a sudden decline or deterioration among pediatric cardiac population?

A. No, I think it is a very common occurrence actually when you are dealing with sick babies that have heart disease.

Q. Why then would you attach any significance to the observation that a child declined suddenly?

A. Because the suddenness and unexpectedness of the event, if you put the two together they will indicate that something wrong may have occurred. Usually when a child deteriorates suddenly, or one would have some idea beforehand that this will occur. Then if you consider the type of heart disease that the child has, the clinical status, whether or not the child had surgery and it may be a postoperative complication or so. If these factors are present then it will be easy to explain the deterioration, and even when it is sudden. On the other hand when they are not present it becomes more difficult to explain. These are the cases that we would include for further investigation.

EE
EMT/PS

Q. You are drawing a distinction, Doctor, between sudden and unexpected. Are you suggesting that a decline may be sudden but it may be expected to occur?

A. Yes.

Q. But if it is sudden and it is not expected to occur, then that raised a flag on your review of these charts?

A. Right. It could be sudden,unexpected or expected. And it could be unexpected but gradual.

Q. Yes.

A. Rather than sudden. So they are two different conditions which I think are useful.

Q. Okay. And then just so that I am sure I follow your methodology in conducting your reviews, having reviewed the clinical picture of each child you then plugged into the assessment as I understand it such digoxin data as were available. At the beginning that wasn't very much. At the end of the summer of 1981 it was a bit more and by 1982 it was a good deal more.

A. Yes.

Q. All right.

A. In addition, we had other

laboratory data such as, for instance, I believe I mentioned earlier the occurrence of renal failure.

Q. Yes.

A. Or no occurrence of renal failure because the child who develops renal failure may retain digoxin and the blood level of the drug may build up over a period of time.

In addition, a child who receives a large dose of digoxin may develop a high level of potassium in the blood and these factors we try and take into consideration.

Q. Now, you also attempted, we know, Dr. Hastreiter, in some cases where toxicological data were available, to form and express an opinion about the size of dose that might have been needed to produce the recorded concentration, the route of administration of such a dose and the time of its administration.

You did that, did you not?

A. Yes. I was specifically asked to do that.

Q. Yes.

A. It is a very difficult thing to do.

Q. I want to deal with the opinions

that you did express as to size of dose when we come to individual cases, but as I understand the evidence that you have given previously, and that is to say at the preliminary inquiry, evidence as to the probable time interval between the administration of digoxin and manifestation of toxic effects, you have said, and Mr. Commissioner this is found in Volume 33 of the preliminary inquiry transcript at Page 25, and also in Volume 34 at Pages 5 to 6.

You have said, Dr. Hastreiter, that in the case of an IV bolus administration of digoxin in a toxic quantity the first effects of toxicity would likely be manifested from 5 to 30 minutes after administration.

A. Yes.

Q. Do you recall having given that evidence?

A. Yes.

Q. Is that still your view?

A. Yes.

Q. You have said, and this is found at Pages 30 to 31 of Volume 33, that in some few cases the onset of toxic effects may be even faster than 5 minutes and in some cases it may take even longer than 30 minutes, but the majority of cases

will begin to manifest the first signs of toxicity within a period of 5 to 30 minutes.

A. Yes.

Q. And I take it, Doctor, that the larger the dose that is administered the sooner, generally speaking, the sooner the toxic effects will begin to appear.

A. That is true.

Q. All right. And you have also said -- this is also found at Page 25 of Volume 33, Mr. Commissioner -- that in the case of oral administration of digoxin in potentially toxic amounts, the first effects of toxicity may appear anywhere from 30 minutes to 2 hours after administration.

A. Yes.

Q. And again with the same observations as with respect to IV: in some cases it will be faster; in some cases longer, but the majority of cases within that time range.

A. Right.

Q. Now, with respect to what you call the first signs or the first manifestations of toxicity, Dr. Hastreiter, I take it they may not even be noticed, they may not be observed.

A. That's true.

Q. The first signs may perhaps be a slowing of the heart rate which if it doesn't trigger a monitor may not be observed at all.

A. Or vomiting. Babies --

Q. Or some vomiting.

A. Babies vomit frequently for many reasons.

Q. Yes. Well, if a baby vomits it is my experience that it is usually noticeable sooner or later.

A. Well, it is noticeable but it is not attributed to digitalis.

Q. That is right. And I take it --

A. The slow heart rate is also noticeable, but it is not attributed to digitalis.

Q. It may not even be noticed is what I am saying of the slow heart rate. It may not be observed at the time it begins to slow, may it?

A. That could be.

Q. It is observable but it may not be observed just by chance.

A. Yes, it could be.

Q. I take it in the case of oral administration the first symptoms may indeed not be noticed because the absorption rate in the case of

oral administration is slower and presumably the signs of toxicity begin to appear rather more subtly, do they?

A. Yes. It is less predictable also.

Q. But do I take it, Dr. Hastreiter, by the time the child suffers a cardiac arrest as a result of digoxin toxicity, some manifestations of toxicity have been present for some period of time. Perhaps a very short period of time or perhaps a longer time, but usually something that has happened prior to the actual arrest.

A. That is true, but as you said yourself, sometimes it is not detected.

Q. It may be a very short interval between an unobserved symptom and arrest.

A. It all depends on how closely the baby is being monitored. For instance, some babies are kept attached to monitors.

Q. Yes.

A. So you can see the electrocardiogram continuously and follow slight changes. On the other hand, if the baby is not being monitored there may be a rather marked change in his heart rate.

Q. Yes.

A. Or rhythm, and one would never detect it.

Q. Nevertheless, Doctor, I take it if one is looking to fix with as much certainty as one can the probable time of administration one should be looking for the first signs of toxicity that appear in a chart.

A. Yes.

Q. Because it is from that time that you are going to measure back your 5 to 30 minutes? That is in the case of IV administration?

A. Yes.

Q. You have also distinguished, Dr. Hastreiter, in the course of your previous evidence between what you call the first toxic effects or the first manifestation of toxicity and peak effects.

You have said, again at Page 25 of Volume 33, Doctor, that after an IV bolus administration of a toxic dose of digoxin the first toxic effects would be manifested from 5 to 30 minutes after administration and the peak effects will occur from 1 to 4 hours after administration.

With respect to oral doses, first effects

30 minutes to 2 hours; peak effect 2 to 6 hours after administration.

Do you recall having given that evidence earlier, Doctor?

A. Yes, sir.

Q. And I take it those are still your views?

A. Yes.

Q. Those I take it are the times within which the dose will have been more or less completely distributed to tissue.

A. Yes.

Q. And they are fairly broad time frames --

A. The peak effects you are talking about?

Q. Yes.

A. Yes.

Q. They are a fairly broad time frame but fairly we have heard a good deal here already about ranges and variability and that sort of time spread doesn't phase us any more, I don't think, Dr. Hastreiter.

A. Yes.

Q. But when you talk about peak

effects, I think I know what that means but I guess I had better be sure.

We are concerned here with the possibility of deaths attributable to digoxin intoxication. I am correct in thinking, am I not, that when you refer in this context to the initial effects of digoxin overdose, you mean the first and in practical terms the first observed toxic effects, the slowing of heart rate, vomiting, perhaps seizure, dysrhythmia, something of that sort?

A. Yes.

Q. Depending on the size of the dose that has been administered, those effects may increase in severity over a period of time, as I understand it?

A. Right.

Q. And if the dose was in a toxic but not a lethal amount, presumably the toxic effects will reach a peak at some point in time and begin to abate presumably?

A. Right.

Q. And it is that peak time that you are talking about when there is maximum concentration, particularly in heart tissue, before there is any significant elimination.

A. Right.

Q. Okay. And that peak effect, as you have said, would occur in the case of IV administration between 1 and 4 hours after dosage; in the case of oral administration, 2 to 6 hours after dosage.

A. Right.

Q. Now, Doctor, if the dose produces what I guess is the ultimate toxic effect; that is to say, death, that in a very real sense is a peak effect but that is not necessarily what you are talking about when you put that time frame on peak effects, is it?

A. No.

Q. Because indeed the death may occur as a result of the accummulation and action of digoxin in heart tissue before there has been total distribution of the digoxin.

A. Right. Before the highest level in the tissue is achieved.

Q. That is right.

A. Right.

Q. That is to say, the overdose administered may be so massive that a sufficient amount of digoxin will be distributed to tissue to

cause death long before the complete alpha phase of distribution has taken place.

A. Right.

Q. All right. And therefore at some more or less early point on the alpha phase of distribution death may occur notwithstanding that the time frame for peak effect has not yet arrived.

A. Right. That is possible.

Q. All right. So therefore, just to be absolutely sure, when you say with respect to an overdose administered by IV that the peak effects will occur 1 to 4 hours after administration, death if the dose is large enough may occur in a shorter time frame.

A. Yes.

Q. And is that why it is important to fix the first signs of toxicity rather than the death because the time it takes to cause death is a bit unknowable, whereas you have been able to give us some kind of a time frame going back from the point of first toxic manifestations.

A. Yes. The only problem, though, it may be very, very difficult to determine the first sign of toxicity.

Q. Of course. On the one hand, you have got death which is a reasonably clearly identifiable event.

A. Easy.

Q. But you don't know what period to work back. In the other case you know the period but it is difficult to identify the event.

A. Right.

Q. It is roundabouts and swings once again in this game, isn't it?

I take it when you say death, are we talking about cardiac arrest or the moment when the child is ultimately pronounced dead?

A. I think cardiac arrest is the better marker because the time of actual pronouncement of death is an artificial, to some degree, situation which could be prolonged with support, life support, although the child is biologically dead; you can keep them breathing or keep the heart pumping or massaging of the heart for long periods of time.

Q. So we should really be focussing more upon the time of arrest?

A. Right.

13

A. And the time the resuscitation team says no more; we can't do anything.

A. Yes. The time of resuscitation can vary. It is usually anywhere from 30 to 60 minutes or so.

Q. Sure.

A. Approximately. But sometimes it can be longer and rarely it can be shorter.

Q. Yes. All right.

MR. LAMEK: Time for the afternoon break?

THE COMMISSIONER: Yes, we will take 15 minutes.

MR. LAMEK: All right. Thank you.

---Short recess.

5dec83
FF
BMcra

--- on resuming.

THE COMMISSIONER: Before I forget. On Wednesday we are going to rise somewhere around twenty to four in the afternoon for reasons peculiar to myself and Commission Counsel, namely, his partner is being Benched.

MR. LAMEK: Q. Dr. Hastreiter, just before we turn to the individual cases that you reviewed, when you came to take account of the digoxin information in making your assessment of these children, I take it that you felt handicapped to some extent by the paucity of the toxicological data that were available to you?

A. Yes.

Q. That is to say that in very many of the children there was no post mortem digoxin information at all and very little in the way of ante mortem therapeutic monitoring levels. Was that your observation?

A. I would say that the therapeutic monitoring was adequate.

Q. Yes.

A. But the post mortem levels were not available in most cases.

Q. And then again in some the only

FF2

post mortem digoxin information available was with respect to exhumed tissues?

A. Yes.

Q. In some you had post mortem digoxin levels in fixed tissues only?

A. Right.

Q. In three children, as I recall it, that is to say, Pacsai, Floryn and Volk, you had digoxin levels -- oh, and Cook as well -- in fresh or frozen tissue?

A. Yes.

Q. And in some, very few, you had digoxin levels in post mortem blood?

A. Yes. Well, these procedures are not routine procedures.

Q. No, of course. And in just two, that is to say, Cook and Pacsai, did you have digoxin levels in blood that was drawn shortly before or within minutes after the cardiac arrest?

A. Yes.

Q. Not a great deal of data to work with, I take it?

A. Right.

Q. We have heard opinions expressed by clinical pharmacologists and by Mr.

FF3

Cimbura that quantitative judgments as to the concentration of digoxin in tissues at the time of death cannot reliably be made on the basis of levels recorded in fixed samples of tissues and a fortiori in exhumed samples of those tissues. Do you agree with those statements?

A. I would agree with the assertion that quantitative measures cannot be made appropriately. I think qualitative determinations have helped us in some cases where these children were not receiving digoxin. I would be very hesitant to try to estimate the amounts --

Q. Sure.

A. -- in fixed specimens.

Q. And in cases therefore other than those where a purely qualitative judgment was of some assistance, and I mean for example, cases where the children had not had digoxin prescribed in life but it was found in their tissues after death, other than those cases where you had no digoxin data upon which you could reasonably make any inference as to levels in life, do I take it that your assessment of the likelihood of digoxin involvement was based essentially upon the clinical picture as disclosed in the chart?

FF4

A. Yes, I think that is correct. There were some exceptions perhaps of a couple of situations where the levels were rather high in either fixed tissue or exhumed tissue and we thought that they correlated well perhaps with the clinical information.

Q. Okay. But in cases where you had to rely only upon the clinical picture with no reliable digoxin data available to you, I take it you were unable to say with any certainty whether digoxin played a part in the deaths of those children?

A. That's true.

Q. The most you could say was that there were elements in the clinical picture which made you suspect that it may have played a part?

A. Right.

Q. Okay. Now, in considering the clinical picture of each child, I take it you formed a judgment about the severity of the child's cardiac condition?

A. Yes.

Q. Was it important to you to do that to enable you to assess whether the arrest was expected or not?

A. Yes, and also to help the other

FF5

investigators.

Q. All right. I am showing to you, Dr. Hastreiter, a list of names of children. There are rather more than the children with whom we are here concerned, but they include all these children and against each child's name there is a numerical score. The legend in the lower right-hand side is Severity Scale of Heart Disease - 10 equals maximum and 1 equals minimum. And it says for Dr. A. Gilmour-Bryson. Did you prepare this sheet?

A. Yes.

Q. Was that based upon your review of the charts and does it represent your assessment of the severity of each child's cardiac condition?

A. Yes.

Q. Does it reflect anything other than cardiac condition?

A. No.

Q. I notice as against Woodcock and against Warner you have noted "other ailments".

A. Yes, I separated -- in parentheses I indicated in these two children, one had severe liver disease and one had severe lung disease and this could have influenced their

FF6

terminal event also.

Q. But the numerical score itself relates solely to cardiac condition?

A. Right.

MR. LAMEK: May that be the next exhibit, please, Mr. Commissioner.

THE REGISTRAR: 281, sir.

THE COMMISSIONER: Yes, 281.

--- EXHIBIT NO. 281: List of children re Severity Scale of Heart Disease.

MR. ORTVED: What is the number opposite Woodcock, Mr. Lamek?

MR. LAMEK: You have a copy of that, do you, Doctor?

THE COMMISSIONER: It is 2 on mine, is it not?

THE WITNESS: I don't have a copy.

MR.LAMEK: It starts with Cook, 8; Woodcock is 2 I believe, is it not.

MR. SCOTT: How about Adamo?

MR. LAMEK: It looks as though it was 3 and then it became 2.

Q. What is Adamo? It has got a 6 and a 7. Is the 6 crossed out?

A. 7, yes.

FF7

Q. Is the 6 crossed out?

A. 7, yes.

Q. It is 7, all right, thank you.

MR. OLAH: Could we perhaps find out why there are two different references to Estrella?

THE COMMISSIONER: Two different references to whom?

MR. OLAH: Estrella.

MR. LAMEK: There are two Estrellas, aren't there? One with 'l' and one with two 'l's.

MR. OLAH: That may account for the difference in the scores. The second one is about six lines from the bottom on the first column.

MR. LAMEK: Yes. The Estrella with whom we are concerned is fourth from the top, is she not, Doctor?

A. Yes.

Q. With a score of 8.

MR. SCOTT: Were there two Estrellas?

MR. LAMEK: Yes, there were two children called Estrella.

THE COMMISSIONER: Were there?

MR. LAMEK: Yes, but one with a single 'l' and one with two 'l's.

THE COMMISSIONER: Oh, yes, all right.

FF(2)
1

MR. LAMEK: We will be referring to that list in the course of the questions if we may, Doctor.

In seeking an explanation of each child's death by considering the clinical picture and course of the child as it was disclosed in the child's chart, you have said that you addressed yourself to medications other than digoxin if in your view such other medications might in some way interfere with the action of digoxin. Were you concerned about medications which might interfere with assay of digoxin?

A. Yes.

Q. And in particular which medications were you concerned about?

A. There was only one really that I was concerned with. There was spironolactone that is found in aldactazide which is a medication which is frequently used amongst this group of patients here.

Q. Was the possible interference of spironolactone with the digoxin assay a matter that you discussed with Mr. Cimbura?

A. Yes.

Q. And were you able to be

FF(2)
2

satisfied that the chance of interference either on his RIA kit or by use of HPLC removed the difficulty?

A. Yes, I think the interference with the RIA method clearly exists but it is a small component of the total determination; with the HPLC I don't think this is a problem.

Q. And further on the question of the other drugs, did you in reading the charts consider the administration of other drugs as perhaps furnishing an occasion for medication errors resulting in the accidental administration of digoxin?

A. I think that has definitely to be considered and the possibility always exists.

Q. Is it a matter to which you addressed your mind however in reviewing the charts?

A. No, I don't think when I reviewed the chart, it was not my function to determine, you know, who did it or how it was done, it was really my function to determine whether it was done, the probability that it had been done

Q. And just one final question on the general part of this, Dr. Hastreiter. Did you feel that being restricted to what was in the clinical

record and not having access to those who treated the children, and obviously without access to the children themselves, did you feel that your ability to form a reliable clinical judgment was significantly impaired?

A. Well, that has to do with the quality of the medical records. I think that in general the quality of the medical records was quite good.

Q. Yes.

A. And I would say that I was not handicapped.

Q. Doctor, can we go then to the individual children? Let us start with the 4 in respect of whose deaths the charges had been laid at the time of your original retainer. May we start with Justin Cook. We know, Dr. Hastreiter, that your evidence in the preliminary inquiry, and it is found, Mr. Commissioner, at Volume 33, pages 52 to 53. You said of Justin Cook that his death was consistent with his clinical condition and cardiac anatomy, but you also said that in your opinion Cook died as a result of what you called a massive digoxin overdose, and you expressed the view, at page 50, that the administration was not accidental.

Are those still your opinions with respect to that child?

A. Yes.

Q. I take it, Doctor, that your opinions with respect to Justin Cook are based largely, if not entirely, on the recorded high concentrations of digoxin in this baby's blood drawn during resuscitation and also post mortem and in the fresh tissues, especially in light of the consideration that digoxin was never prescribed for him. Were those the main bases for the opinions that you formed about this child?

A. Yes.

Q. Is there anything else that serves as a basis for your opinions about Justin Cook?

A. Well, perhaps I should explain that on the clinical grounds Justin Cook's death would be an expected death because the child had a very severe type of heart problem and had what appeared to be a cyanotic episode on the day before his death and I would not at all have been surprised that he would have died from his original condition. But it is the toxicological data later that pointed to it, the digoxin, as the cause of death.

Q. I am interested, Dr. Hastreiter,

that when we look at your 1982 review of Cook, it is found at page 72 of the binder, upon a review of the clinical picture you assess as fair the probability of his having received a massive digoxin overdose. In light of what you have just told me, that is to say, that his clinical condition was such that his death really was not unexpected at all, why would you even rate that as a fair probability in light of the clinical picture?

A. Because I could not totally exclude it. The only ones that I have excluded and categorized as small were those where an obvious reason for the death was there, existence, such as children who died in the operating room or who died as a consequence of a complication of surgery or something that really was obvious.

This was I think highly the probability that Justin Cook's heart defect contributed to his death on clinical grounds was high, was a high probability, but I don't think that we can completely forget the possibility that he was intoxicated. Of course, at that time I already knew the toxicology and I may have been influenced by it.

Q. Yes, I understand.

A. I tried to be as unbiased as I

6

could with regard to toxicology but I knew already that he had very high levels and that may have influenced me a little bit.

/DM/ak

Q. I take it that you are satisfied that the strong probability is that digoxin intoxication caused the death of this child?

A. Yes.

Q. And we know that on a severity scale of 1 to 10 you rated him as an 8, and that as I take it you have suggested indicates that in your view he had a very severe cardiac problem?

A. Right.

Q. And we know that on the day preceding his death he had had a cardiac catheterization?

A. Yes, he was an emergency cardiac catheterization.

Q. And indeed surgery was scheduled for the next day?

A. Right.

Q. The day indeed of his death?

A. Right.

Q. And that again was on an emergency basis?

A. Yes.

Q. With respect to the blue spell, the cyanotic spell at 6 o'clock on the evening preceding his death, Doctor, do you suggest that that

G2

was a product of digoxin intoxication?

A. No, I don't.

Q. That was a problem of his cardiac condition, was it?

A. Right.

Q. In your view?

A. Yes.

Q. Clearly the child had a pretty tenuous hold on life, did he not?

A. Yes.

Q. I take it, Doctor, that the opinion that you hold on digoxin killed this baby, has to involve an interpretation of, or an influence drawn from the digoxin levels recorded in his blood and especially the fresh tissues. And second, some opinion as to the amount of digoxin he received, and when he received it?

A. Yes, he was not supposed to have received any.

Q. That's right. Can we look first at the interpretation of the digoxin concentration levels? Am I right in thinking, Dr. Hastreiter, that the most important piece of digoxin information about Justin Cook, is the one as to concentrations in fresh tissue, and this is

G3

a matter upon which you and I may differ.

A. In my opinion the confirmation of a high concentration in the blood pre-mortem as well as post mortem, and the high concentration in fresh tissue makes this a very solid situation. I think the tissue without the blood alone would not be as strong a case; and the blood without the tissue would probably be even a weaker case. The combination I think is what makes it very strong in my opinion, and I feel that the blood is very important, especially the pre-mortem blood.

Q. I understand, Doctor, and I confess that my question is more directed to cases that we will come to later than it is to the particular case of Justin Cook.

In Cook we do at least have digoxin information of the two kinds, blood as you say post morten and ante mortem, and fresh tissue.

Is it fair, Doctor, that the availability of the fresh tissue concentrations is what gives essentially meaning to the blood level?

A. I think everybody would agree that the effects of digitalis, that the actions of digitalis occur in the heart, and the heart is a receptor organ and a target organ for the drug.

G4

However, with respect to measurements of digitalis, or digoxin in myocardium, there is a great deal of controversy among the experts really as to the value of this measurement, especially because of the spread of the variability of the measurements. The fact that not only this has got a good correlation between the clinical course and the myocardium concentration of the drug. I think in Justin Cook's case, however, because the level was so extremely high it becomes very significant. If it were in an intermediate range, it probably would have been very difficult to interpret. If it were a very low level then it may have significance in the opposite direction.

Q. Yes, of course. Doctor, are you aware of any recorded case in the literature where in fresh heart tissue a level of 1170 was recorded in a patient who survived?

A. No, I am not aware of one. I am only aware of another infant in whom a level over 1,000 was recorded and this is the case that we reported and the child dying.

Q. Is it fair to say then, Doctor, that if you had the fresh heart tissue concentration, but through some freak accident did

G5

not have a blood level, you could still place a fairly solid inference upon the fresh heart tissue concentration?

A. If the level were above a thousand I would.

Q. As it was in Cook's case?

A. Yes, as it was in Cook's case.

Q. And I guess what I am suggesting to you is this, Doctor; if on the other hand all you had was the blood level without any indication of tissue concentration, particularly in Justin Cook, where no prior digoxin had apparently been administered, certainly none was prescribed, it would be virtually impossible for you to say whether the recorded blood level represented a very early stage of alpha phase distribution, or some subsequent stage of distribution, would it not?

A. I think that is always a very important consideration. However, from a practical standpoint I think if you look at the blood levels obtained in a clinical setting, children who are alive, as well as autopsy, and children who were receiving digoxin and had blood levels drawn at autopsy; if you look at the reported cases in the literature of children who were killed by digoxin,

G6

you will see that the only times where high levels of this magnitude 70 or so are encountered are instances where very, very large doses were given.

I think theoretically it is possible, certainly, that if one were to sample very early following the administration, even giving relatively small over doses, one would have a very high level, but that only lasts for a very short period of time and I think it would be, in practice, very unlikely that such a situation would occur with such a high level. If the level was 10 or 12, or 15, it would be a different story.

Q. Is not the significance of the fixed heart tissue - I am sorry, the fresh heart tissue concentration this, that it precludes even the very small likelihood that the 72 nanogram level represented a level immediately post-administration?

A. In Justin Cook's case certainly, I think this is a very important confirmation of the existence of a massive overdose.

Q. Because it requires a period of time to have elapsed between dosage and death to have permitted distribution to the extent that was recorded in the fresh heart tissue, does it not?

A. That's right. The half time

G7

of uptake of the digoxin by the myocardium from the blood is approximately half an hour when the drug is given intravenously. So that if we had a level of 1,000, let's say, and if this is - if the drug was given half an hour earlier, that means his ultimate level would have been 2,000, but you are reaching half of the expected maximum myocardium concentration at that particular time. It does help you predict the time to some degree.

Q. And it precludes the possibility of administration immediately prior to death?

A. Yes, it does, because there would not have been time enough for it to accumulate in the myocardium.

Q. And without the information as to the fresh tissue levels, I take it all you would have been able to do from the blood level alone would be to draw an inference of more or less compelling validity as to the probable time of administration; you can do that with a little more comfort knowing there had been time for distribution, can you not?

A. Yes.

Q. But as you say in Cook's case the two pieces of information feed each other?

A. Right.

G8

Q. I want to come back to that same area however, Dr. Hastreiter, when I come to some of the other children, where essentially all we have is a blood level, without any fresh tissue measurements?

A. Yes.

Q. Let us stay with Justin Cook, your opinion is that Justin Cook, some time before his death received what you called a massive overdose of digoxin; and then in your best judgment the toxicity produced by that overdose killed him?

A. Right.

Q. That is the bottom line of your view at this time, is that right?

A. Yes.

Q. I am interested of course in your opinions as to the time of administration, the route of administration and the size of the overdose. If you look at the binder, at page 74, one sees at the end of the long paragraph almost at the bottom of the page:

"If one assumes that the infant was given one large dose of intravenous digoxin, the most likely time for this to have occurred would have been just

G9

"prior to the infant's terminal deterioration at 3:30 hours."

And the top of the next page:

"It would have been extremely difficult for the infant to have maintained a plasma level of digoxin of about 70 nanograms per millilitre for any sustained period of time without the development of fatal disturbances of the heart rhythm and death. This is the basis for my statement that, assuming that the laboratory values are correct, digoxin was given shortly before the infant's terminal episode of deterioration on 22/3/81."

And I take it those statements represent your opinion today as well?

A. Yes.

Q. With respect to the route of administration on page 75, following the passage I have just read, Dr. Hastreiter, you reported:

"There are several possibilities as to how the overdose of digoxin was administered."

And you then list them and discount them one by one:

G10

"By mouth - this is unlikely because it would have required a large amount and would have been difficult to administer unless the infant had a gastro-intestinal tube in place.

Slow intravenous infusion - such as adding the drug to the IV bag or bottle. This is also unlikely since, because of the dilution effect and the slow rate of administration, it would take a long time for the blood concentration of digoxin to reach 70 nanograms."

And I take it part of that thinking, Dr. Hastreiter, is that if the drug were infusing slowly then probably long before the blood level reached 70 the child would have succumbed to the effects?

A. That is correct.

Q. And third:

"By IV 'bolus' - such as rapid injection of the drug into the IV tubing. This is a more likely possibility."

Doctor, does any one of those three possible routes, include the oral administration of

G11

the parenteral preparation?

A. No, I don't think I specifically indicated this possibility, although it exists. I think it is not a good one, but it should be considered.

Q. Where under Item 1 you were referring to oral administration, I take it what you had in mind was oral administration of the elixir?

A. Yes, because the large amount does not apply to the parenteral administration, it would be a relatively small amount.

Q. Yes. I take it you can administer the parenteral preparation orally?

A. Yes.

Q. As between oral administration of parenteral preparation and IV bolus injection, do you have an opinion as to which was the more likely route of administration in this case?

A. The oral administration of the parenteral versus the IV injection, the intravenous?

Q. Yes.

A. I think the intravenous is better because you can more easily achieve the level of this magnitude. The oral administration although

G12

it could be concentrated, using the parenteral medication, I do not feel that it can be ruled out but I think that is less likely to have occurred than the other one.

Q. Thank you. Now, Dr. Hastreiter, Mr. Cimbura has reported, and this Mr. Commissioner, is in Exhibit 95A at page 3, a reference to Sample T20, and let me show you this, Dr. Hastreiter, Mr. Cimbura has reported on Sample T20 and this is from Justin Cook, it was:

> "Sample of thick fluid material in a jar bearing a seal number. Labelled 'small bowel content March 24/81 Justin Cook...'".

And then the officer's name:

> "Reported to be part of small bowel and content."

And he reported that in that material he found a total, not a concentration, but a total of 621 nanograms of digoxin.

HH
EMT/PS

I would ask if that report has any significance insofar as your opinion is concerned that the most likely route of administration was by intravenous bolus injection?

A. I don't think it helps really because it is my understanding that this material was the total content that could be obtained from the bowel.

Q. Yes.

A. And the amount, the total amount would be 620 nanograms, and this is really not a very large amount for the entire bowel.

It is well known that when the drug is given intravenously it is excreted through the bowel to some degree, and it is found in the bowel, and certainly the bile -- it is reabsorbed in the bowel producing a so-called entero hepatic cycle, but, no, it doesn't surprise me. It doesn't help, I don't believe.

If we had a very large concentration and if we perhaps could measure the amount -- could determine that there was a very large amount of let's say a milligram or more in the bowel, lumen itself, perhaps would indicate it had been given via the GI tract, but this does not.

Q. All right, thank you.

Could we turn to the probable time of administration? You have said in your report and I have read it to you, in your best opinion the overdose was probably administered shortly before the child's terminal event.

Would it be of assistance to you to have a copy of the chart at this time, Doctor?

A. Perhaps.

MR. LAMEK: I wonder, Mr. Registrar, if Dr. Hastreiter could have a copy of Justin Cooke's chart, please? It is Exhibit 116.

MR. OLAH: While my friend is getting the material, I wonder if he would assist by asking the converse side of the question and ask namely whether the absence of digoxin in the small bowel content assists in ruling out oral administration.

MR. LAMEK: That I take it is a hypothetical question because there was some found there, wasn't there?

MR. OLAH: Sorry?

MR. LAMEK: As a hypothetical question because there was some found there.

MR. OLAH: Whether the amount found rules out the mode of administration.

MR. LAMEK: Okay.

MR. OLAH: I don't know if it assists.

MR. LAMEK: Okay.

Q. Doctor, let me ask you this then: I take it that if we contemplate oral administration, if we assume oral administration, then I take it you would be putting earlier in time the probable time of administration.

A. Yes.

Q. Okay. To what point in time?

A. It isn't easy to answer this question. I think it could be maybe a matter of half an hour or an hour earlier, but --

Q. All right.

A. -- very difficult to pinpoint.

Q. Perhaps 2:30 or something of that order rather then?

A. Could be.

Q. Had this dose of the parenteral preparation been administered orally at 2:30, would you have expected to find more digoxin reported in the small bowel sample?

A. Not necessarily. Not necessarily.

Q. All right. And therefore your

report of the finding in the small bowel is totally neutral; it neither bespeaks oral administration nor precludes it.

A. In my opinion it is.

Q. Thank you.

Now looking for the time of administration on the assumption that we are dealing here with an intravenous bolus injection, I ask you, Dr. Hastreiter, what record is the first recorded indications in the chart of digoxin toxicity, and the nursing notes, if they are of assistance to you, start at Page 26. There is Nurse Nelles' note covering the period from 2:30 onwards on Page 29, and from the period 7 p.m. of the 21st of March to 3 a.m. on the 22nd is on Page 28. Or indeed any other place in the chart you can recall anything that would be of help to us in fixing as best we can the first signs of toxicity in this child as you interpret them.

A. I see a note here on Page 27 which says -- it is dated 22-3-81. That was the date of his death; right?

Q. Yes.

A. That is in fact the arrest note, the nursing notes having been completed later

in time.

A. Oh, okay, because here it says 5 hours and then 5:10 so it's 5:10 so that is just out of order here.

Q. Yes. That is a question I think of the sequence in which the notes were actually recorded.

A. Yes. So it says the baby was stable from 21 to 23 hours; between 23 and 2:30 slept well.

Q. You are looking at Page 28, Doctor?

A. Yes, 28.

Q. The nursing note on the lower half of the page?

A. Right.

Q. Yes.

A. And the respirations seemed easy and regular. The right leg being mottled and cold to touch is related to the cardiac catheterization problem and has no bearing on the baby's general condition I don't think.

Nutrition says that the baby tolerated two feedings at 2030 and at 2:30 respectively of D5W, etc.

Then the next page, Page 29 we have another note dated 22-81 -- March 22, 1981, slept well after 2:30 feeding; rested comfortably until about 3:45 when hands were noted to be more cyanosed.

O2 was increased to 100%; vital signs were started when baby began to have a seizure. So this must be the earliest indication of the problem.

Q. Of a problem which you would suspect as being related to digoxin intoxication?

A. I suspect so because the baby never recovered from this episode and died, and had very high digoxin levels at that particular time.

Q. So the first recorded thing that you would look to then is the increased cyanosis observed in the hands at 3:45 and the seizure?

A. Yes. This is what is listed in the chart.

Q. Doctor, is seizure activity a known, albeit a nonspecific symptom of digoxin intoxication?

A. Seizure activity can be caused

by many, many different factors. However, it is also a finding in massive digitalis intoxication. It can be.

Q. And is recorded in the literature, is it?

A. Oh, yes.

Q. So if we look to 3:45 as being roughly the time of the first recorded symptom that you would suspect to be associated with digoxin intoxication, and we are looking for time of administration, may I take it that on the range that you gave us, 5 to 30 minutes prior to that, we are looking at a probable time of administration somewhere between 2:45 -- sorry, 3:15 and perhaps 3:30, 3:40, something of that sort.

A. Yes.

Q. 3:30, 3:40. Between 3:15 and 3:40.

A. And 3:40, yes.

Q. Now, does the rapidity with which events progressed after that initial problem at 3:45 progressed right through to arrest and ultimately death cause you any misgiving about your identifying the incident at 3:45 as the first recorded sign of toxicity, or does that rapid course

fortify your view?

A. I think as I mentioned earlier the baby was kept alive until 4:56.

Q. Yes.

A. But that, of course, has a great deal to do with the vigour of the resuscitation efforts, and I am sure that they tried very hard to keep this baby alive.

The baby was probably not viable some time before then, and it is difficult to establish at what time the baby actually died. He was pronounced dead at 4:56. I don't think it, you know, helps or detracts --

Q. All right.

A. -- from the idea of the drug having been given at that particular time.

Q. We know that the Code 25 for the arrest was called at 4:20.

A. Right.

Q. And that, Doctor, would be approximately an hour from the kind of time frame for administration that we talked about a couple of minutes ago: 3:15 to 3:40.

A. Yes.

Q. Arrest at 4:20.

A. It would fit into the scheme, the schedule, quite well, I think.

Q. And would that period of time, that is to say from somewhere between 3:15 and 3:40 until 4:20 or shortly thereafter in your opinion afford sufficient time for the degree of distribution of digoxin to tissue to occur that is recorded in Mr. Cimbura's reports?

A. This would have been approximately --

Q. Approximately an hour we are talking.

A. No, we are talking about an hour and a half if it were at 3:15 it could have been --

Q. To 4:20.

A. Oh, to 4:20.

Q. Was the arrest. I suppose, Doctor, we would say there was impaired circulation at best after the time of arrest.

A. Yes, but the distribution may have continued subsequently for some time, and the myocardial sample was obtained later.

Q. Yes.

A. Death was at 4:56. So it could

have been two hours or it could have been at least --

Q. An hour and a half?

A. Hour and a half.

Q. Three half lives is what we are talking about?

A. Yes, which would be adequate assuming that the baby was given a very large dose.

Q. Yes.

A. In other words in one hour there should have been 75% of the ultimate predicted level in the myocardium.

Q. Yes.

A. In an hour and a half it would be 87-1/2% and in half an hour would have been only 50%.

Q. 50%?

A. That means that the ultimate level would have been 2,000 which would mean that the dose was very, very massive.

Q. Okay, Doctor, we have dealt then with your best view of the probable route of administration and time of administration.

I am coming, Mr. Commissioner, to the size of the dose and we are getting into some rather complicated calculations. Is this an appropriate

time to break for the day?

THE COMMISSIONER: Perhaps we had better rise now until 10:00 tomorrow morning.

MR. LAMEK: Thank you, sir.

---Whereupon, the hearing was adjourned at 4:35 until 10:00 on Tuesday, December 6, 1983.